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Replication of KCNJ11 (p.E23K) and ABCC8 (p.S1369A) association in Russian diabetes mellitus 2 type cohort and meta-analysis

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Abstract

© 2015 Sokolova et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. The genes ABCC8 and KCNJ11 have received intense focus in type 2 diabetes mellitus (T2DM) research over the past two decades. It has been hypothesized that the p.E23K (KCNJ11) mutation in the 11p15.1 region may play an important role in the development of T2DM. In 2009, Hamming et al. found that the p.1369A (ABCC8) variant may be a causal factor in the disease; therefore, in this study we performed a meta-analysis to evaluate the association between these single nucleotide polymorphisms (SNPs), including our original data on the Siberian population (1384 T2DM and 414 controls). We found rs5219 and rs757110 were not associated with T2DM in this population, and that there was linkage disequilibrium in Siberians (D'=0.766, r2= 0.5633). In addition, the haplotype rs757110[T]- rs5219[C] (p.23K/p.S1369) was associated with T2DM (OR = 1.52, 95% CI: 1.04-2.24). We included 44 original studies published by June 2014 in a meta-analysis of the p.E23K association with T2DM. The total OR was 1.14 (95% CI: 1.11-1.17) for p.E23K for a total sample size of 137,298. For p.S1369A, a meta-analysis was conducted on a total of 10 studies with a total sample size of 14,136 and pooled OR of 1.14 [95% CI (1.08-1.19); p = 2 × 10-6]. Our calculations identified causal genetic variation within the ABCC8/KCNJ11region for T2DM with an OR of approximately 1.15 in Caucasians and Asians. Moreover, the OR value was not dependent on the frequency of p.E23K or p.S1369A in the populations.

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